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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,839	04/17/2008	Roy H. Larsen	50147/008002	1058

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
05/20/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/588,839	LARSEN ET AL.	
	Examiner	Art Unit	
	JAGADISHWAR SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/15/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-11 and 15-17 in the reply filed on 02/18/2011 is acknowledged. The traversal is on the ground(s) that the special technical feature linking the presently amended claim 1 does not describe hydroxyapatite and request of withdrawal of the restriction requirement. This is not found persuasive because, group I is drawn to composition and group II and III are drawn to process for preparing and a method of radioachemical treatment of a human which imposes search burden on the examiner. Claims 12-14 and 24-29 have been withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 08/15/2007 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

The drawings were received on 08/08/2006. These drawings are acknowledged

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deutsh et al (US 5,609,850) in view of Michael R. McDevitt et al (European Journal of Nuclear Medcine, Vol. 25(9), 1341-1351, 1998).

Claims are drawn to hydroxyapatite (HA) incorporating an alpha-emitting radionuclide selected from group consisting of ^{211}At, ^{212}Bi, ^{223}Ra, ^{224}Ra, ^{225}Ac and ^{227}Th or an in vivo generator for an alpha-emitting radionuclide selected from the group consisting of the beta-emitting radionuclide ^{212}Pb, ^{211}Pb, ^{213}Bi, and ^{225}Ra, wherein HA is particulate and has a size in the range of 1 nm to 100 micron and surface modified with amino acids, peptides, proteins or a combination thereof.

Deutsh teaches a composition comprising apatite particles for medical diagnsotic imaging. The apatite particles include hydroxyapatite (sometimes refereed to as hydroxylapatite), fluoroapatite, carbonate apatite and mixtures thereof (col. 1 lines 50-55). Typical particle sizes are in the range from about 10 nm to about 50 microns (col. 1 lines 63-65). The apatite particles may be incorporated with paramagnetic species

(metal ions) such as iron , chromium, manganese to improve magnetic resonance and radiopaque heavy metal such as bismuth, hafnium , lanthanum and the lanthanides to provide x-ray constrast (col. 2 lines 44-50 and col. 6 lines 46-50). The apatite particles may be stabilized with coating agents such as alcohols and polyalcohols compounds (reads on polyethylene glycol), biomolecules such as peptides, proteins, antibodies, and lipids. Such coating agents stabilize the small apatite particles by reducing further particle growth and promoting particle suspension (col. 8 lines 15-26). Additional disclosure includes that the stabilized apatite particles are desirable for in vivo use as medical diagnostic composition comprising pharmaceutically acceptable carriers.

Deutsh fails to teach specifically radionuclide selected from group consisting of ^{211}At, ^{212}Bi, ^{223}Ra, ^{224}Ra, ^{225}Ac and ^{227}Th.

Michael teaches the application of alpha-emitting radionuclides (particles) in targeted radioimmunotherapy. The radionuclides include ^{211}At, ^{212}Bi, ^{223}Ra, ^{225}Ac and ^{212}Pb (abstract). Additional disclosure includes that using alpha-emitting radioimmunoconugates for therapy in vivo, the rapid delivery of the short-lived isotope to targets was assured, without significant exchange of the radioconstruct from the peritoneal cavity to the systemic circulation affecting normal tissue toxicity (page 1348).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate alpha-emitting radionuclide such as ^{211}At, ^{212}Bi, ^{223}Ra, ^{225}Ac and ^{212}Pb into Deutsh composition. The person of ordinary skill in the art would have been motivated to make those modifications because Micheal teaches that teaches that alpha-emitters have considerably shorter half-lives than the commonly

used beta-emitters and relevant pharmacokinetic information will be obtained if imaging and/or sampling starts immediately after administration (page 1346) and the cytotoxicity induced by alpha-emitter is far more selective. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success because both Deutsh and Michael teaches a composition for improved medical diagnostic imaging agents that can be used in the same field of endeavor such as to provide adequate visualization, to a warm blooded animal either systemically or locally to an organ or tissues to be imaged.

Claims 1-11 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over McMillan et al (US 5,300,281) in view of Line et al (US 2004/0258614) and Atcher et al (US 4,970,062).

Claims are drawn to hydroxyapatite (HA) incorporating an alpha-emitting radionuclide selected from group consisting of ^{211}At, ^{212}Bi, ^{223}Ra, ^{224}Ra, ^{225}Ac and ^{227}Th or an in vivo generator for an alpha-emitting radionuclide selected from the group consisting of the beta-emitting radionuclide ^{212}Pb, ^{211}Pb, ^{213}Bi, and ^{225}Ra, wherein HA is particulate and has a size in the range of 1 nm to 100 micron and surface modified with amino acids, peptides, proteins or a combination thereof.

McMillan teaches a radioactive composition containing a pharmaceutically acceptable carrier a chelate sorbed to a calcific matrix and layer mixed metal hydroxide used for treating arthritis and other diseases (abstract and col. 2 lines 47-54). The calcifc matrix is a complex phosphate of calcium such as hydroxyapatite (col. 3 lines 29-31). The calcific matrix includes surface modification by the presence of ions such as

carbonate, magnesium and substitution of other elements such as carbon for potassium, and fluoride for hydroxyl (reads on fluorine). The calcific matrices are particulate in nature, the particles being spherical having an average diameter of between about 1 and about 90 microns (col. 3 lines 38-51). The chelating agents such as cyclic polyaminophosphonate and linear polyamino phosphonates (reads on phosphonates) sorbed to the calcific matrix (col. 6 lines 14-51). The radionuclides include beta emitting metals with half-lives of from about 2 hours to about 7 days (col. 3 lines 52-65). Additional disclosure includes that stabilized radiolabeled calcific matrix (solid or liquid form) is useful for therapeutic radiation ablation treatment methods, such as for the treatment of arthritis.

McMillan fails to teach specifically radionuclide selected from group consisting of ^{211}At, ^{212}Bi, ^{223}Ra, ^{224}Ra, ^{225}Ac and ^{227}Th.

Line teaches a pharmaceutical composition comprising microscopic radioactive particles in physiologically acceptable liquid for injection into human (0038). The particulate material comprising biocompatible microspheres have alpha, beta or gamma emitting radionuclide attached to surface (0056). Therapeutic radionuclides include Bi-213, At-211 (0176). The microparticles can be provided with inert pharmaceutically acceptable carrier and/or formulating agents and/or adjuvants, stabilization aid such as cysteine (aminoacid) gentisic acid, and inositol (reads on organic compounds, 0192), solubilization aid such as glycerin, polyethylene glycol (0184 and 0194). Additional disclosure includes preparation of aqueous compositions that contains an active

ingredient as injectables, either as liquid solutions or suspensions, solid forms suitable for solution in, or suspensions in or other form of a fluid (0208).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate alpha-emitting radionuclides into McMillan's radioactive composition. The person of ordinary skill in the art would have been motivated to make those modifications because Line teaches that coupling of alpha emitter radionuclides to microsphere particles allow the delivery of high intensity tumoricidal doses of radiation without exposure of normal liver tissue (0040). As evidenced by Atcher et al (US 4,970,062, herein after '062), clinically alpha emitting radionuclides have the potential to be more efficacious than other beta-emitting radionuclides. In comparison to beat-emitters, it is estimated that alpha irradiation has one-hundredth the range and may have up to ten times the energy deposition per unit path length making it more efficient in killing a tumor cell while perhaps sparing normal cells, or for that matter, to any organ ('062 see col. 5 lines 39-50). Therefore, one of ordinary skill in the art would have had a reasonable expectation of success because both McMillan and Line teaches a composition comprising microscopic radioactive particles that can be used in the same field of endeavor such as for radiation ablation treatments, for example in the treatment of arthritis, particularly rheumatoid arthritis.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. S./
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618